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Research Article

Dynamics of a Fractional Order HIV Infection Model with Specific Functional Response and Cure Rate

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We propose a fractional order model in this paper to describe the dynamics of human immunodeficiency virus (HIV) infection. In the model, the infection transmission process is modeled by a specific functional response. First, we show that the model is mathematically and biologically well posed. Second, the local and global stabilities of the equilibria are investigated. Finally, some numerical simulations are presented in order to illustrate our theoretical results.

1. Introduction

Fractional order differential equations (FDEs) are a generalization of ordinary differential equations (ODEs) and they have many applications in various fields such as mechanics, image processing, viscoelasticity, bioengineering, finance, psychology, and control theory [1–7]. In addition, it has been deduced that the membranes of cells of biological organisms have fractional order electrical conductance [8].

Modeling by FDEs has more advantages to describe the dynamics of phenomena with memory which exists in most biological systems, because fractional order derivatives depend not only on local conditions but also on the past. More precisely, calculating the time-fractional derivative of a function $f(t)$ at some time $t = t_1$ requires all the previous history, that is, all $f(t)$ from $t = 0$ to $t = t_1$. In addition, the region of stability of FDEs is larger than that of ODEs. Moreover, some previous study compared between the results of the fractional order model, the results of the integer model, and the measured real data obtained from 10 patients during primary HIV infection [9]. This study proved that the results of the fractional order model give predictions to the plasma virus load of the patients better than those of the integer model.

From the above biological and mathematical reasons, we propose a fractional order model to describe the dynamics of HIV infection that is given by

$$\begin{aligned} D^{\alpha}T(t) &= \lambda - dT - \frac{\beta TV}{1+\alpha_1 T+\alpha_2 V+\alpha_3 TV} + \rho I, \\ D^{\alpha}I(t) &= \frac{\beta TV}{1+\alpha_1 T+\alpha_2 V+\alpha_3 TV} - (a+\rho)I, \\ D^{\alpha}V(t) &= kI - \mu V, \end{aligned} \tag{1}$$

where $T(t)$, $I(t)$, and $V(t)$ represent the concentrations of uninfected $CD4^+$ T-cells, infected cells, and free virus particles at time t, respectively. Uninfected cells are assumed to be produced at a constant rate λ, die at the rate dT, and become infected by a virus at the rate $\beta TV/(1 + \alpha_1 T + \alpha_2 V + \alpha_3 TV)$, where $\alpha_1, \alpha_2, \alpha_3 \geq 0$ are the saturation factors measuring the psychological or inhibitory effect. Infected cells die at the rate aI and return to the uninfected state by loss of all covalently closed circular DNA (cccDNA) from their nucleus at the rate ρI. Free virus particles are produced from infected cells at the rate kI and cleared at the rate μV.

The fractional order derivative used in system (1) is in the sense of Caputo. We use this Caputo fractional derivative for

two reasons: the first reason is that the fractional derivative of a constant is zero and the second reason is that the initial value problems depend on the integer order derivative only. In addition, we choose $0 < \alpha \leq 1$ in order to have the same initial conditions as ODE systems.

On the other hand, system (1) generalizes many special cases existing in the literature. For example, when $\alpha_1 = \alpha_2 = \alpha_3 = 0$, we get the model of Arafa et al. [10]. Further, we obtain the model of Liu et al. [11] when $\alpha_3 = 0$. It is very important to note that when $\alpha = 1$, system (1) becomes a model with an ordinary derivative which is the generalization of the ODE models presented in [12–15].

The rest of the paper is organized as follows. In the next section, we give some preliminary results. In Section 3, equilibria and their local stability are investigated. In Section 4, the global stability of the two equilibria is established. Numerical simulations of our theoretical results are presented in Section 5. Finally, the paper ends with conclusion in Section 6.

2. Preliminary Results

We first recall the definitions of the fractional order integral, Caputo fractional derivative, and Mittag-Leffler function that are given in [16].

Definition 1. The fractional integral of order $\alpha > 0$ of a function $f : \mathbb{R}_+ \to \mathbb{R}$ is defined as follows:

$$I^{\alpha} f(t) = \frac{1}{\Gamma(\alpha)} \int_0^t (t-x)^{\alpha-1} f(x)\, dx, \tag{2}$$

where $\Gamma(\cdot)$ is the Gamma function.

Definition 2. The Caputo fractional derivative of order $\alpha > 0$ of a continuous function $f : \mathbb{R}_+ \to \mathbb{R}$ is given by

$$D^{\alpha} f(t) = I^{n-\alpha} D^n f(t), \tag{3}$$

where $D = d/dt$ and $n - 1 < \alpha \leq n, n \in \mathbb{N}$.

In particular, when $0 < \alpha \leq 1$, we have

$$D^{\alpha} f(t) = \frac{1}{\Gamma(1-\alpha)} \int_0^t \frac{f'(x)}{(t-x)^{\alpha}} dx. \tag{4}$$

Definition 3. Let $\alpha > 0$. The function E_{α}, defined by

$$E_{\alpha}(z) = \sum_{j=0}^{\infty} \frac{z^j}{\Gamma(\alpha j + 1)}, \tag{5}$$

is called the Mittag-Leffler function of parameter α.

Let $f : \mathbb{R}^n \to \mathbb{R}^n$ with $n \geq 1$. Consider the fractional order system

$$\begin{aligned} D^{\alpha} x(t) &= f(x), \\ x(t_0) &= x_0, \end{aligned} \tag{6}$$

with $0 < \alpha \leq 1$, $t_0 \in \mathbb{R}$, and $x_0 \in \mathbb{R}^n$. For the global existence of solution of system (6), we need the following lemma.

Lemma 4. *Assume that f satisfies the following conditions:*

(i) *$f(x)$ and $(\partial f/\partial x)(x)$ are continuous for all $x \in \mathbb{R}^n$.*

(ii) *$\|f(x)\| \leq \omega + \lambda\|x\|$ for all $x \in \mathbb{R}^n$, where ω and λ are two positive constants.*

Then, system (6) has a unique solution on $[t_0, +\infty)$.

The proof of this lemma follows immediately from [17]. For biological reasons, we assume that the initial conditions of system (1) satisfy

$$\begin{aligned} T(0) &= \phi_1(0) \geq 0, \\ I(0) &= \phi_2(0) \geq 0, \\ V(0) &= \phi_3(0) \geq 0. \end{aligned} \tag{7}$$

In order to establish the nonnegativity of solutions with initial conditions (7), we need also the following lemmas.

Lemma 5 (see [18]). *Suppose that $g(t) \in C[a,b]$ and $D^{\alpha} g(t) \in C[a,b]$ for $0 < \alpha \leq 1$; then, one has*

$$g(t) = g(a) + \frac{1}{\Gamma(\alpha)} D^{\alpha} g(\xi) (t-a)^{\alpha}, \quad a < \xi < t, \ \forall t \in (a,b]. \tag{8}$$

Lemma 6 (see [18]). *Suppose that $g(t) \in C[a,b]$ and $D^{\alpha} g(t) \in C[a,b]$ for $0 < \alpha \leq 1$. If $D^{\alpha} g(t) \geq 0$ $\forall t \in [a,b]$, then $g(t)$ is nondecreasing for each $t \in [a,b]$. If $D^{\alpha} g(t) \leq 0$ $\forall t \in [a,b]$, then $g(t)$ is nonincreasing for each $t \in [a,b]$.*

Theorem 7. *For any initial conditions satisfying (7), system (1) has a unique solution on $[0, +\infty)$. Moreover, this solution remains nonnegative and bounded for all $t \geq 0$. In addition, one has*

(i) *$N(t) \leq N(0) + \lambda/\delta$,*

(ii) *$V(t) \leq V(0) + (k/\mu)\|I\|_{\infty}$,*

where $N(t) = T(t) + I(t)$ and $\delta = \min\{a, d\}$.

Proof. It is easy to see that the vector function of system (1) satisfies the first condition of Lemma 4. It remains to prove the second condition. Let

$$X(t) = \begin{pmatrix} T(t) \\ I(t) \\ V(t) \end{pmatrix}, \quad \zeta = \begin{pmatrix} \lambda \\ 0 \\ 0 \end{pmatrix}. \tag{9}$$

To this end, we discuss four cases:

(i) If $\alpha_1 \neq 0$, then system (1) can be written as follows:

$$D^{\alpha} X(t) = \zeta + A_1 X + \frac{\alpha_1 T}{1 + \alpha_1 T + \alpha_2 V + \alpha_3 TV} A_2 X, \tag{10}$$

where

$$A_1 = \begin{pmatrix} -d & \rho & 0 \\ 0 & -(a+\rho) & 0 \\ 0 & k & -\mu \end{pmatrix},$$

$$A_2 = \begin{pmatrix} 0 & 0 & -\dfrac{\beta}{\alpha_1} \\ 0 & 0 & \dfrac{\beta}{\alpha_1} \\ 0 & 0 & 0 \end{pmatrix}. \tag{11}$$

Moreover, we have

$$\left\|D^\alpha X(t)\right\| \le \|\zeta\| + \left(\|A_1\| + \|A_2\|\right)\|X\|. \tag{12}$$

(ii) If $\alpha_2 \neq 0$, we have

$$D^\alpha X(t) = \zeta + A_1 X + \frac{\alpha_2 T}{1+\alpha_1 T + \alpha_2 V + \alpha_3 TV} A_3 X, \tag{13}$$

where

$$A_3 = \begin{pmatrix} 0 & 0 & -\dfrac{\beta}{\alpha_2} \\ 0 & 0 & \dfrac{\beta}{\alpha_2} \\ 0 & 0 & 0 \end{pmatrix}. \tag{14}$$

Then,

$$\left\|D^\alpha X(t)\right\| \le \|\zeta\| + \left(\|A_1\| + \|A_3\|\right)\|X\|. \tag{15}$$

(iii) If $\alpha_3 \neq 0$, we have

$$D^\alpha X(t) = \zeta + A_1 X + \frac{\alpha_3 TV}{1+\alpha_1 T + \alpha_2 V + \alpha_3 TV} A_4, \tag{16}$$

where

$$A_4 = \begin{pmatrix} -\dfrac{\beta}{\alpha_3} \\ \dfrac{\beta}{\alpha_3} \\ 0 \end{pmatrix}. \tag{17}$$

Then,

$$\left\|D^\alpha X(t)\right\| \le \left(\|\zeta\| + \|A_4\|\right) + \|A_1\|\|X\|. \tag{18}$$

(iv) If $\alpha_1 = \alpha_2 = \alpha_3 = 0$, we have

$$D^\alpha X(t) = \zeta + A_1 X + V A_5 X, \tag{19}$$

where

$$A_5 = \begin{pmatrix} -\beta & 0 & 0 \\ \beta & 0 & 0 \\ 0 & 0 & 0 \end{pmatrix}. \tag{20}$$

Then,

$$\left\|D^\alpha X(t)\right\| \le \|\zeta\| + \left(\|V\|\|A_5\| + \|A_1\|\right)\|X\|. \tag{21}$$

Thus, the second condition of Lemma 4 is satisfied. Then, system (1) has a unique solution on $[0, +\infty)$. Next, we show that this solution is nonnegative. From (1), we have

$$\begin{aligned} D^\alpha T(t)\big|_{T=0} &= \lambda + \rho I \ge 0, \\ D^\alpha I(t)\big|_{I=0} &= \frac{\beta TV}{1+\alpha_1 T + \alpha_2 V + \alpha_3 TV} \ge 0, \\ D^\alpha V(t)\big|_{V=0} &= kI \ge 0. \end{aligned} \tag{22}$$

According to Lemmas 5 and 6, we deduce that the solution of (1) is nonnegative.

Finally, we prove that the solution is bounded. By adding the first two equations of system (1), we get

$$D^\alpha N(t) \le \lambda - \delta N(t). \tag{23}$$

Hence,

$$N(t) \le N(0) E_\alpha\left(-\delta t^\alpha\right) + \frac{\lambda}{\delta}\left[1 - E_\alpha\left(-\delta t^\alpha\right)\right]. \tag{24}$$

Since $0 \le E_\alpha(-\delta t^\alpha) \le 1$, we have

$$N(t) \le N(0) + \frac{\lambda}{\delta}. \tag{25}$$

The third equation of system (1) implies that

$$\begin{aligned} V(t) = {} & V(0) E_\alpha\left(-\mu t^\alpha\right) \\ & + k \int_0^t I(s)\, \alpha (t-s)^{\alpha-1} \frac{dE_\alpha}{ds}\left(-\mu (t-s)^\alpha\right) ds. \end{aligned} \tag{26}$$

Then,

$$V(t) \le V(0) E_\alpha\left(-\mu t^\alpha\right) + \frac{k\|I\|_\infty}{\mu}\left(1 - E_\alpha\left(-\mu t^\alpha\right)\right). \tag{27}$$

Consequently,

$$V(t) \le V(0) + \frac{k\|I\|_\infty}{\mu}. \tag{28}$$

This completes the proof. □

3. Equilibria and Their Local Stability

It is easy to see that system (1) always has a disease-free equilibrium $E_0(\lambda/d, 0, 0)$. Therefore, the basic reproduction number of our system (1) is given by

$$R_0 = \frac{k\beta\lambda}{\mu(a+\rho)(d+\lambda\alpha_1)}. \tag{29}$$

Biologically, this basic reproduction number represents the average number of secondary infections produced by one infected cell during the period of infection when all cells are uninfected. Further, it is not hard to get the following result.

Theorem 8. *(i) If $R_0 \le 1$, system (1) has a unique disease-free equilibrium of the form $E_0(T_0, 0, 0)$, where $T_0 = \lambda/d$. (ii) If $R_0 > 1$, the disease-free equilibrium is still present and system (1) has a unique chronic infection equilibrium of the form $E_1(T_1, (\lambda - dT_1)/a, k(\lambda - dT_1)/a\mu)$, where $T_1 = 2(a+\rho)(a\mu+\alpha_2\lambda k)/(ak\beta+(a+\rho)(\alpha_2 dk-\alpha_1 a\mu-\alpha_3 k\lambda)+\sqrt{\overline{\delta}})$ with*

$$\begin{aligned}\overline{\delta} &= \left(ak\beta + (a+\rho)\left(\alpha_2 dk - \alpha_1 a\mu - \alpha_3 k\lambda\right)\right)^2 \\ &\quad + 4\alpha_3 kd\,(a+\rho)^2\left(a\mu + \alpha_2\lambda k\right).\end{aligned} \tag{30}$$

Next, we investigate the local stability of equilibria. Let $E_e(T, I, V)$ be an arbitrary equilibrium of system (1). Then, the characteristic equation at E_e is given by

$$\begin{vmatrix} -d - V\dfrac{\partial f}{\partial T} - \xi & \rho & -V\dfrac{\partial f}{\partial V} - f(T,V) \\ V\dfrac{\partial f}{\partial T} & -(a+\rho) - \xi & V\dfrac{\partial f}{\partial V} + f(T,V) \\ 0 & k & -\mu - \xi \end{vmatrix} = 0, \tag{31}$$

where

$$f(T,V) = \frac{\beta T}{1 + \alpha_1 T + \alpha_2 V + \alpha_3 TV}. \tag{32}$$

We recall that the equilibrium E_e is locally asymptotically stable if all roots ξ_i of (31) satisfy the following condition [19]:

$$\left|\arg(\xi_i)\right| > \frac{\alpha\pi}{2}. \tag{33}$$

Theorem 9. *(i) If $R_0 < 1$, then E_0 is locally asymptotically stable. (ii) If $R_0 > 1$, then E_0 is unstable.*

Proof. Evaluating (31) at E_0, we have

$$(d+\xi)\left[\xi^2 + (a+\rho+\mu)\,\xi + \mu(a+\rho)(1-R_0)\right] = 0. \tag{34}$$

Obviously, the roots of (34) are

$$\begin{aligned}\xi_1 &= -d, \\ \xi_2 &= \frac{-(a+\rho+\mu) - \sqrt{(a+\rho+\mu)^2 - 4\mu(a+\rho)(1-R_0)}}{2}, \\ \xi_3 &= \frac{-(a+\rho+\mu) + \sqrt{(a+\rho+\mu)^2 - 4u(a+\rho)(1-R_0)}}{2}.\end{aligned} \tag{35}$$

It is clear that ξ_1 and ξ_2 are negative. However, ξ_3 is negative if $R_0 < 1$ and it is positive if $R_0 > 1$. Therefore, E_0 is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$. □

Now, we focus on the local stability of the chronic infection equilibrium E_1. It follows from (31) that the characteristic equation at E_1 is given by

$$P(\xi) := \xi^3 + a_1\xi^2 + a_2\xi + a_3 = 0, \tag{36}$$

where

$$\begin{aligned}a_1 &= \mu + d + a + \rho + \frac{\beta V_1(1+\alpha_2 V_1)}{(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)^2}, \\ a_2 &= d(\mu + a + \rho) \\ &\quad + \frac{\beta V_1\left[(a+\mu)(1+\alpha_2 V_1) + kT_1(\alpha_2+\alpha_3 T_1)\right]}{(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)^2}, \\ a_3 &= \frac{\beta V_1\left[a\mu(1+\alpha_2 V_1) + kdT_1(\alpha_2+\alpha_3 T_1)\right]}{(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)^2}.\end{aligned} \tag{37}$$

It is obvious that $a_1 > 0$, $a_2 > 0$, and $a_3 > 0$. Further, we have

$$\begin{aligned}a_1 a_2 - a_3 &= a\left(d(\mu+a+\rho) + \frac{\beta V_1\left[a(1+\alpha_2 V_1) + kT_1(\alpha_2+\alpha_3 T_1)\right]}{(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)^2}\right) \\ &\quad + d\left(d(\mu+a+\rho) + \frac{(a+\mu)\beta V_1(1+\alpha_2 V_1)}{(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)^2}\right) + \left(\mu+\rho + \frac{\beta V_1(1+\alpha_2 V_1)}{(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)^2}\right)h_2 > 0.\end{aligned} \tag{38}$$

So, Routh–Hurwitz conditions are satisfied. Let $D(P)$ denote the discriminant of the polynomial P given by (36); then,

$$D(P) = 18a_1a_2a_3 + (a_1a_2)^2 - 4a_3a_1^3 - 4a_2^3 - 27a_3^2. \tag{39}$$

Using the results in [19], we easily obtain the following result.

Theorem 10. *Assume that $R_0 > 1$.*

(i) *If $D(P) > 0$, then E_1 is locally asymptotically stable for all $\alpha \in (0, 1]$.*

(ii) *If $D(P) < 0$ and $\alpha < 2/3$, then E_1 is locally asymptotically stable.*

4. Global Stability

In this section, we study the global stability of the disease-free equilibrium E_0 and the chronic infection equilibrium E_1.

Theorem 11. *If $R_0 \le 1$, then the disease-free equilibrium E_0 is globally asymptotically stable.*

Proof. Define Lyapunov functional $L_0(t)$ as follows:

$$L_0(t) = \frac{T_0}{1+\alpha_1 T_0}\Phi\left(\frac{T}{T_0}\right) + \frac{\rho}{2(1+\alpha_1 T_0)(a+d)T_0}(T - T_0 + I)^2 + \frac{a+\rho}{k}V, \tag{40}$$

where $\Phi(x) = x - 1 - \ln(x)$, $x > 0$. Calculating the derivative of $L_0(t)$ along solutions of system (1) and using the results in [20], we get

$$D^\alpha L_0(t) \le \frac{1}{1+\alpha_1 T_0}\left(1 - \frac{T_0}{T}\right)D^\alpha T + D^\alpha I \cdot \frac{\rho}{(1+\alpha_1 T_0)(a+d)T_0}(T - T_0 + I) \cdot (D^\alpha T + D^\alpha I) + \frac{a+\rho}{k}D^\alpha V. \tag{41}$$

Using $\lambda = dT_0$, we obtain

$$\begin{aligned} D^\alpha L_0(t) &\le -\frac{d(T-T_0)^2}{(1+\alpha_1 T_0)T} - \frac{1}{1+\alpha_1 T_0}\left(1 - \frac{T_0}{T}\right)f(T,V)V \\ &\quad + \frac{\rho}{1+\alpha_1 T_0}\left(1 - \frac{T_0}{T}\right)I + f(T,V)V \\ &\quad - \frac{d\rho(T-T_0)^2}{(a+d)T_0(1+\alpha_1 T_0)} \\ &\quad - \frac{a\rho I^2}{(a+d)T_0(1+\alpha_1 T_0)} \\ &\quad + \frac{\rho}{T_0(1+\alpha_1 T_0)}I(T_0 - T) - \frac{(a+\rho)\mu}{k}V, \end{aligned} \tag{42}$$

$$\begin{aligned} D^\alpha L_0(t) &\le -\left(\frac{1}{T} + \frac{\rho}{(a+d)T_0}\right)\frac{d(T-T_0)^2}{1+\alpha_1 T_0} \\ &\quad - \frac{\rho I(T-T_0)^2}{TT_0(1+\alpha_1 T_0)} - \frac{a\rho I^2}{(a+d)T_0(1+\alpha_1 T_0)} \\ &\quad + \frac{(a+\rho)\mu}{k}(R_0 - 1)V \\ &\quad - \frac{\beta T_0(\alpha_2 + \alpha_3 T)}{(1+\alpha_1 T_0)(1+\alpha_1 T + \alpha_2 V + \alpha_3 TV)}V^2. \end{aligned}$$

Hence, if $R_0 \le 1$, then $D^\alpha L_0(t) \le 0$. Furthermore, it is clear that the largest invariant set of $\{(T, I, V) \in D : D^\alpha L_0(t) = 0\}$ is the singleton $\{E_0\}$. Therefore, by LaSalle's invariance principle [21], E_0 is globally asymptotically stable. □

Theorem 12. *The chronic infection equilibrium E_1 is globally asymptotically stable if $R_0 > 1$ and*

$$R_0 \le 1 + \frac{d(a+\rho)(\lambda\alpha_2 k + a\mu) + \rho\lambda^2\alpha_3 k}{\rho\mu(a+\rho)(d+\lambda\alpha_1)}. \tag{43}$$

Proof. Define Lyapunov functional $L_1(t)$ as follows:

$$\begin{aligned} L_1(t) &= \frac{1+\alpha_2 V_1}{1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1}T_1\Phi\left(\frac{T}{T_1}\right) \\ &\quad + I_1\Phi\left(\frac{I}{I_1}\right) + \frac{a+\rho}{k}V_1\Phi\left(\frac{V}{V_1}\right) \\ &\quad + \frac{\rho(1+\alpha_2 V_1)}{2T_1(a+d)(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)}(T \\ &\quad - T_1 + I - I_1)^2. \end{aligned} \tag{44}$$

Then, we have

$$\begin{aligned} D^\alpha L_1(t) &\le \frac{1+\alpha_2 V_1}{1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1}\left(1 - \frac{T_1}{T}\right) \\ &\quad \cdot D^\alpha T + \left(1 - \frac{I_1}{I}\right)D^\alpha I \\ &\quad \cdot \frac{\rho(1+\alpha_2 V_1)}{T_1(a+d)(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)}(T - T_1 \\ &\quad + I - I_1)(D^\alpha T + D^\alpha I) + \frac{a+\rho}{k}\left(1 - \frac{V_1}{V}\right)D^\alpha V. \end{aligned} \tag{45}$$

Using $\lambda = dT_1 + aI_1$, $f(T_1, V_1)V_1 = (a+\rho)I_1$, $\mu/k = I_1/V_1$, and $1 - f(T_1,V_1)/f(T,V_1) = ((1+\alpha_2 V_1)/(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1))(1 - T_1/T)$, we get

$$\begin{aligned} D^\alpha L_1(t) &\le d\left(1 - \frac{f(T_1,V_1)}{f(T,V_1)}\right)(T_1 - T) + (a+\rho) \\ &\quad \cdot I_1\left(4 - \frac{f(T_1,V_1)}{f(T,V_1)} - \frac{I_1}{I}\frac{V}{V_1}\frac{f(T,V)}{f(T_1,V_1)} - \frac{I}{I_1}\frac{V_1}{V}\right. \\ &\quad \left. - \frac{f(T,V_1)}{f(T,V)}\right) + (a+\rho)I_1\left(-1 - \frac{V}{V_1} + \frac{f(T,V_1)}{f(T,V)}\right. \\ &\quad \left. + \frac{V}{V_1}\frac{f(T,V)}{f(T,V_1)}\right) \\ &\quad - \frac{d\rho(1+\alpha_2 V_1)}{T_1(a+d)(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)}(T \\ &\quad - T_1)^2 \\ &\quad - \frac{a\rho(1+\alpha_2 V_1)}{T_1(a+d)(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)}(I - I_1)^2 \\ &\quad - \frac{\rho(1+\alpha_2 V_1)}{TT_1(1+\alpha_1 T_1 + \alpha_2 V_1 + \alpha_3 T_1 V_1)}(T - T_1)^2(I \\ &\quad - I_1). \end{aligned} \tag{46}$$

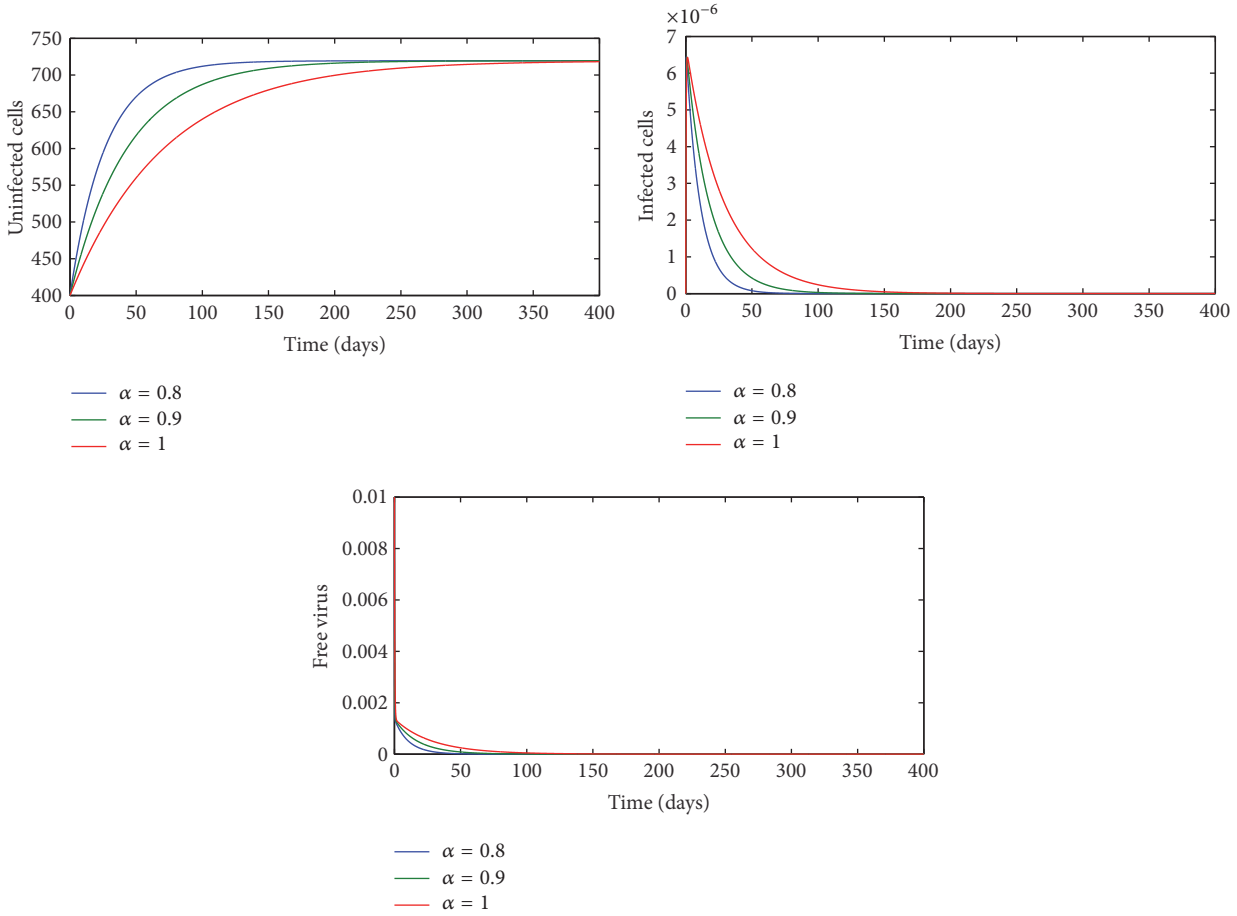

FIGURE 1: Stability of the disease-free equilibrium E_0.

Thus,

$$
\begin{aligned}
&D^{\alpha}L_1(t)\\
&\le -\frac{(1+\alpha_2V_1)(T-T_1)^2}{TT_1(1+\alpha_1T_1+\alpha_2V_1+\alpha_3T_1V_1)}\left((dT_1-\rho I_1)\right.\\
&\left.+\frac{d\rho T}{d+a}+\rho I\right)-(a+\rho)I_1\\
&\cdot\frac{(1+\alpha_1T)(\alpha_2+\alpha_3T)(V-V_1)^2}{V_1(1+\alpha_1T+\alpha_2V+\alpha_3TV)(1+\alpha_1T+\alpha_2V_1+\alpha_3TV_1)} \quad (47)\\
&-(a+\rho)I_1\left(\Phi\left(\frac{f(T_1,V_1)}{f(T,V_1)}\right)+\Phi\left(\frac{I_1}{I}\frac{V}{V_1}\frac{f(T,V)}{f(T_1,V_1)}\right)\right.\\
&\left.+\Phi\left(\frac{I}{I_1}\frac{V_1}{V}\right)+\Phi\left(\frac{f(T,V_1)}{f(T,V)}\right)\right)\\
&-\frac{a\rho(1+\alpha_2V_1)}{T_1(a+d)(1+\alpha_1T_1+\alpha_2V_1+\alpha_3T_1V_1)}(I-I_1)^2.
\end{aligned}
$$

It is clear that $\Phi(x) \ge 0$. Consequently, $D^{\alpha}L_1(t) \le 0$ if $dT_1 \ge \rho I_1$. In addition, it is easy to see that this condition is equivalent to (43). Further, the largest invariant set of $\{(T,I,V) \in D : D^{\alpha}L_1(t) = 0\}$ is the singleton $\{E_1\}$. By LaSalle's invariance principle, E_1 is globally asymptotically stable. □

It is important to see that

$$
\lim_{\rho\to 0}\frac{d(a+\rho)(\lambda\alpha_2k+a\mu)+\rho\lambda^2\alpha_3k}{\rho\mu(a+\rho)(d+\lambda\alpha_1)}=+\infty. \quad (48)
$$

According to Theorem 12, we obtain the following result.

Corollary 13. *The chronic infection equilibrium E_1 is globally asymptotically stable when $R_0 > 1$ and ρ is sufficiently small.*

5. Numerical Simulations

In this section, we give some numerical simulations in order to illustrate our theoretical results. We discretize system (1) by using fractional Euler's method presented in [22]. Firstly, we take the parameter values as shown in Table 1.

By calculation, we have $R_0 = 0.9283 < 1$. Then, system (1) has a disease-free equilibrium $E_0(719.4245, 0, 0)$. By Theorem 11, the solution of (1) converges to E_0 (see Figure 1). Consequently, the virus is cleared and the infection dies out.

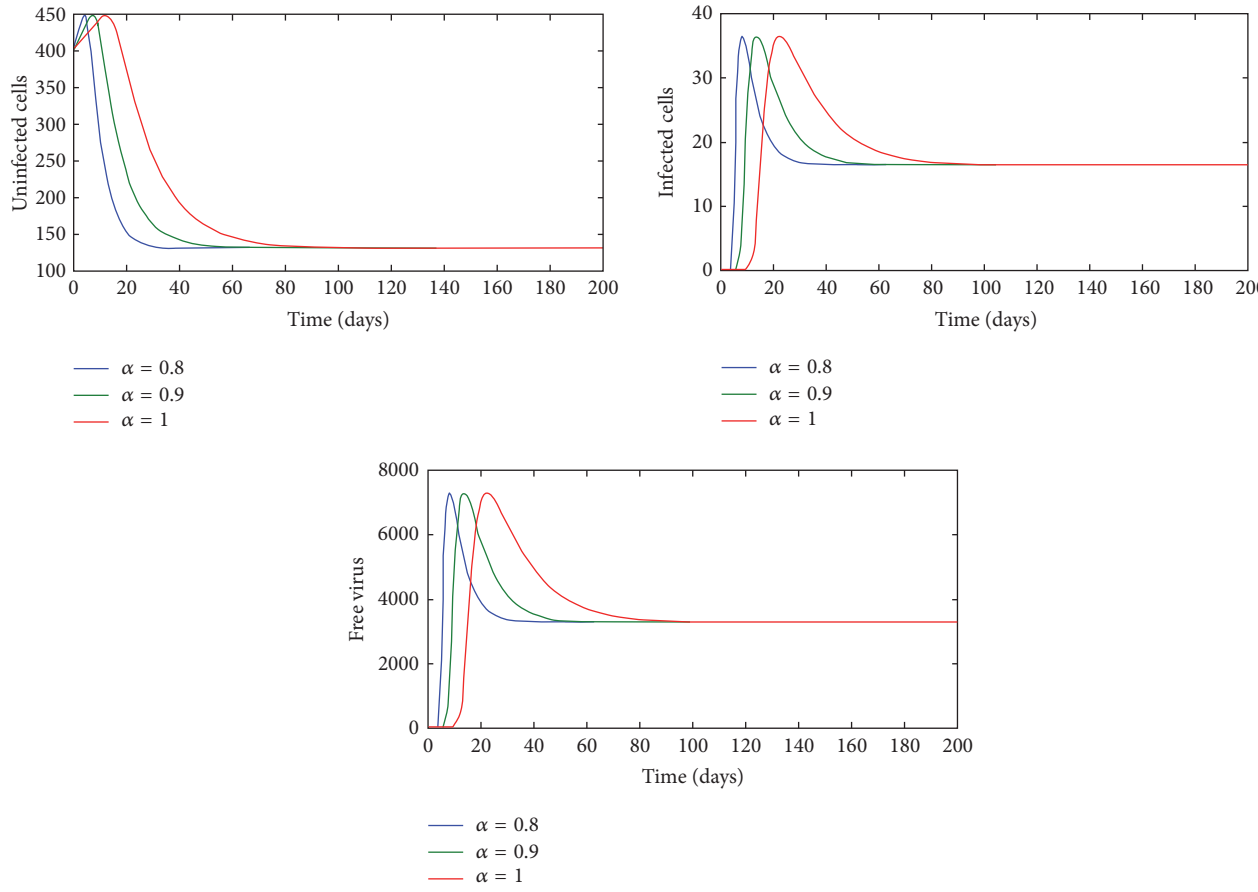

Figure 2: Stability of the chronic infection equilibrium E_1.

Table 1: Parameter values of system (1).

Parameters	Values
λ	10
d	0.0139
β	0.00024
ρ	0.01
a	0.5
k	600
u	3
α_1	0.1
α_2	0.01
α_3	0.00001

Now, we choose $\beta = 0.001$ and we keep the other parameter values. In this case, $R_0 = 3.8678$ and

$$1 + \frac{d(a+\rho)(\lambda\alpha_2 k + a\mu) + \rho\lambda^2\alpha_3 k}{\rho\mu(a+\rho)(d+\lambda\alpha_1)} = 415.885. \quad (49)$$

Hence, condition (43) is satisfied. Therefore, the chronic infection equilibrium $E_1(130.1613, 16.3815, 3276.3)$ is globally asymptotically stable. Figure 2 demonstrates this result.

6. Conclusion

In this paper, we have proposed a fractional order model of HIV infection with specific functional response and cure rate. This functional response covers the most functional responses used by several authors such as the saturated incidence rate, the Beddington-DeAngelis functional response, and the Crowley-Martin functional response. We have shown that the proposed model has a bounded and nonnegative solution as desired in any population dynamics. By using stability analysis of fractional order system, we have proved that if the basic reproduction number $R_0 \leq 1$, the disease-free equilibrium E_0 is globally asymptotically stable for all $\alpha \in (0, 1]$, which means that the virus is cleared and the infection dies out. However, when $R_0 > 1$, the disease-free equilibrium E_0 becomes unstable and there exists another biological equilibrium, namely, chronic infection equilibrium E_1, that is globally asymptotically stable provided that condition (43) is satisfied. In this case, the HIV virus persists in the host and the infection becomes chronic. Furthermore, we have remarked that if the cure rate ρ is equal to zero or is sufficiently small, condition (43) is satisfied and the global stability of E_1 is only characterized by $R_0 > 1$.

According to the above theoretical analysis, we deduce that the global dynamics of the model are fully determined by the basic reproduction number R_0. In addition, we see

that the fractional order parameter α has no effect on the global dynamics of our model, but it can affect the time for arriving at both steady states (see Figures 1 and 2). Moreover, the fractional order model and main results presented by Liu et al. in [11] are generalized and improved.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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